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CORTICOSTEROIDS BY TRANSCORTIN IN PLASMA

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THE EFFECT OF PHYSICAL EXERCISE ON BINDING OF  
CORTICOSTEROIDS BY TRANSCORTIN IN PLASMA

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ABSTRACT. The content of protein-bound and free forms of 11-OCS, and also the binding capacity of transcortin were examined in 11 healthy highly-qualified athletes who were in condition of chronic physical overexertion during the examination; 12 healthy untrained men were also observed (control group). Determinations were made in the state of rest and during four-day veloergometric exercises. During rest the processes of steroid-protein interaction in healthy athletes coursed normally; this caused a considerable prevalence of transcortin-bound fraction over the free form of the hormones. As to athletes with a chronic physical overexertion, a disturbance of the activity of globulin binding with corticosteroids, even in the state of rest, led to an elevation of biologically active forms of the hormones in the blood. During maximal physical exertion healthy athletes displayed a reduction of transcortin-binding capacity in vitro, to the level of protein-bound corticosteroids in the blood of persons investigated. In athletes with a chronic physical overexertion there were revealed stable changes in transcortin-binding capacity, which led to increase in biologically active forms of 11-OCS in the blood both during muscular exertion and prolonged rest.

Possible mechanisms involved in development of the mentioned changes are discussed.

The content of biologically active corticosteroids in the blood is determined by two basic factors: the secretory activity of the cortico matter of the adrenal glands, and by the reaction of the steroids secreted into the blood stream with the specific corticosteroid binding globulin — transcortin.

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\*Numbers in the margin indicate pagination of the foreign text.

Reacting with the hormones, transcortin exerts a significant influence on the rate of entry of corticosteroids into the cells, on the intensity of metabolism, on the rate of their elimination from the organism, and, through the secretion of ACTH, on their synthesis by the adrenal cortex. In binding the corticosteroids, globulin locks them out of the sphere of physiological action.

A study of the processes of steroid-transcortin reaction enables one to take a new approach to estimating the functional condition of the adrenal cortex.

#### Materials and Methods.

Determining the content of protein-bound (primarily with transcortin) and free forms of 11-OCS in the blood plasma was carried out by the method of gel filtration, developed by DeMoor et al., [1], and modified in the Interclinical Hormonal Laboratory of the First Moscow Medical Institute [2]. The method was based upon the capacity of dextran gel — sefadeks — during the filtration of plasma through it to separate the hormones into two fractions: those bound with protein and the free forms. Processing of the obtained fractions and their measurement was conducted after the method of Yu. A. Pankov and I. Ya. Usvatova [3].

We investigated two groups of athletes. The first group included 11 healthy, highly-qualified athletes ranging in age from 18 to 26; the second group included 18 qualified athletes in the age group 18 to 28 who were occupied with various types of sports and among whom, at the time of examination, there were objective signs of chronic physical overexertion [4, 5]. In the capacity of a control, 12 healthy men ranging in age from 18 to 26 were examined; these men had not earlier been regularly involved in sports.

The binding capacity of transcortin in vitro, the content of protein bound and free forms of 11-OCS in the plasma of the subjects were determined both in a state of calm and under conditions of a four-day bicycle ergometer exercise. Exercise on each of the four days consisted on three "trips". In each "trip", the work carried out was gradually increased with respect to load. The blood for examination on the first and fourth days was taken

immediately after exercise, on the third day in the morning, before exercise. Among the healthy athletes, blood was not investigated after physical exercise on the first day.

### Results and Their Discussion.

According to the results of the investigations which were conducted, the binding capacity of transcortin in vitro among healthy untrained persons averages  $28.3 \pm 0.6$  mkg%, while among healthy athletes it is  $28.3 \pm 2.2$  mkg%, i.e., no differences in the binding activity of globulin among the subjects of these two groups were observed (see the table). This is in agreement with the data of the literature and the data obtained earlier by us among practically healthy people. The binding capacity of transcortin in athletes with chronic physical overexertion turned out to be reliably diminished in comparison with the same measurement in the control group and among the healthy athletes (on the average  $24.0 \pm 0.8$  mkg%;  $P < 0.001$ ).

Among healthy untrained people, the total concentration (protein-bound and free forms) of 11-OCS in the blood, in a state of rest, comprised, on the average,  $23.8 \pm 0.95$  mkg%, which corresponded to the data of the literature and to the results of the determination of these indices earlier made by us among practically healthy people. Here the relationship between fractions of hormones in the blood was 1-8.7. Among healthy athletes, the level of total 11-OCS in the blood somewhat exceeded their content in the control group, reaching, on the average,  $26.9 \pm 1.7$  mkg% ( $P > 0.2$ ); the content of transcortin bound corticosteroids in the blood among these persons was  $23.6 \pm 1.2$  mkg%. The given magnitude is significantly higher than the corresponding index in the control group ( $P < 0.001$ ). This is probably caused by the nearly normal concentration of biologically active forms of steroids: the relationship between fractions of hormones among these was 1-7.9, or nearly does not differ from the relationship of the fractions among practically healthy people. /15

Among athletes with chronic physical overexertion, at the same level of total corticosteroids in the blood, the content of free fractions of hormones had undergone a two-fold increase in comparison with their concentration in the control group, and exceeded by 1.7 times that level among healthy athletes,

being, on the average,  $5.5 \pm 1.0$  mkg%. The relationship between fractions of hormones among them was 1-3.9, which indicated an increase in the concentration of biologically active forms of steroids.

A comparison of the indices of binding capacity of transcortin in vitro, with the content of corticosteroids bound with the given globulin, in the blood of healthy people and in the blood of trained athletes shows that the level of binding in vitro predominates over that in the plasma, which is characteristic for binding processes in the condition of physiological rest. When comparing these same magnitudes in athletes with chronic physical overexertion, no reliable difference between them was detected.

Hence, among healthy athletes in a condition of physiological rest, processes of steroid-protein reaction occur normally, which is responsible for the significant dominance of the transcortin bound fraction over the free fraction of hormones. Among athletes with chronic physical overexertion, even in the state of rest, the decrease in intensity of binding corticosteroids by globulin leads to an increase of the blood content of biologically active forms of hormones.

On the first day of physical exertion, the binding capacity of transcortin in vitro among untrained persons somewhat diminished, comprising, on the average,  $25.6 \pm 2.6$  mkg%, however, this decrease is statistically unreliable ( $P > 0.05$ ). However, in a majority of people the content of corticosteroids in the blood plasma, in response to physical exertion, increases; the concentration of hormones bound with transcortin did not change in comparison with their level in a state of rest, which also led to an increase in the content of biologically active forms. This was a three-fold increase (to  $6.4 \pm 1.7$  mkg%). Here, the equilibrium of fractions of hormones in the blood was displaced toward an increase in the free forms: their relationship was 1-2.9. In the period of restoration, i.e., in the morning after the second day of exercise, the binding capacity of transcortin in vitro (three persons) was 28.8 mkg%, which corresponded to the normal indices. The total content of 11-OCS in the blood did not change in comparison with the same index in the period of exercise, remaining at a somewhat heightened level; no changes in the concentration of protein-bound and free forms of hormones was observed (see the table), thanks to which

the relationship between fractions of corticosteroids remained at the previous level. The data of comparing the indices of binding capacity of transcortin with the concentration of transcortin-bound corticosteroids indicate that the binding capacity under conditions of integrity of the organism is not realized, not withstanding the fact that the concentration of hormones in the blood increases. In connection with this, the overall content of corticosteroids in the blood increases only at the expense of the free forms of hormones. The data obtained by us enable one to consider that the maximal physical exercise in untrained people leads to an increase in the secretory activity of the adrenal cortex, thanks to which an increase in the secretion of free, biologically active forms of corticosteroids into the blood stream occurs; these biologically active forms of corticosteroids, apparently, bring about the reaction of adaptation in response to physical exercise. /16

Among healthy athletes, physical exercise caused a decrease in the binding capacity of transcortin, whose magnitude on the fourth day, after concluding the "trips" reached  $21.5 \pm 2.3$  mkg%, which corresponded to the content of protein-bound corticosteroids among them in their blood (see the table). It should be noted that the binding capacity of transcortin was clearly decreased among the subjects of this group. In the period of recovery, on the morning of the third day, an increase in the binding capacity of globulin was observed; on the average this went to  $25.1 \pm 1.5$  mkg%. However, its magnitude did not reach the indices which were obtained in the starting condition, i.e., in the period of long-term rest. The difference of this increase indicates a tendency to normalization of the steroid-protein reaction in the period of recovery. The content of total 11-OCS in the blood plasma during this process remain practically unchanged, being on the average  $21.3 \pm 2.0$  mkg%. The level of protein free hormones also did not change and was  $2.6 \pm 0.5$  mkg%.

Hence, among healthy athletes in the period of maximum physical exercise, the binding capacity of transcortin in vitro decreased, and its magnitude reached the level of protein-bound corticosteroids in the blood of the subjects. This indicates that in the process of physical exercise the volume of globulin decreases, but in the period of rest it becomes restored normal values. As the result of such factors, there is a decrease in the binding capacity of protein,

which cannot now be exactly explained. An investigation of the content of 11-OCS and their protein-bound and free forms in the plasma after the conclusion of exercise (on the fourth day), did not reveal any quantitative changes of these values in comparison with the period of recovery and in a condition of rest.

The obtained data enable one to hypothesize that in a majority of healthy athletes physical exercise does not cause significant activation of the functions of the adrenal cortex. The content of biologically active forms of 11-OCS does not practically change throughout the course of this entire period.

Among athletes with chronic physical overexertion, maximum physical stress led to a decrease in the binding capacity of transcortin, which was caused during the investigation on both the first and the fourth day after finishing the "trips". It should be noted that in the course of the entire period of observations these indices remained at the same level (see the table). A comparison of the obtained data with the results of determining the binding capacity of transcortin in the period of recovery and in a state of rest detected a firm change in the binding capacity of corticosteroid binding globulin in the subjects of this group. We find confirmation of this fact when comparing the cited data with the level of protein-bound corticosteroids in the blood: however, the differences found were not reliable ( $P > 0.05$ ).

The total level of 11-OCS in the blood in the period of exercise corresponded to the upper limit of fluctuations of normal values, comprising, respectively,  $26.0 \pm 2.5$  and  $25.4 \pm 2.0$  mkg% after the first and fourth days of exercise. The concentration of protein-bound steroids here remained at almost the same level as in the state of rest ( $19.6 \pm 2.7$  and  $19.9 \pm 1.2$  mkg% respectively). As a result, the level of free biologically active forms of the hormones remained high, exceeding their content in the blood of healthy athletes in the period of bicycle ergometric exercise and corresponding to these values among untrained people. The dynamic equilibrium of fractions of hormones in the blood changed toward the free forms of corticosteroids.

An analysis of the indices of binding capacity of transcortin, of the content of protein-bound and free forms of corticosteroids in the period of



recovery (morning of the third day) indicates, first, an absence of changes in the above-mentioned indices over this period in comparison with the period of rest, and secondly, correspondence in a majority of cases of the obtained results to the data of determining these values in untrained people. Hence, among athletes in whom there are objective signs of chronic physical overexertion, one notes a decrease in the binding capacity of transcortin, which leads to an increase of blood contents of biologically active forms of 11-OCS both in the period of muscular exercise and in the state of rest. /17

### Conclusions.

1. Among healthy athletes in a state of physiological rest, the indices of binding capacity of transcortin correspond to the norm, while among athletes with chronic physical overexertion they decrease.

2. During maximal physical exertion among healthy athletes, the capacity of globulin to bind hormones has a tendency to decrease and recovers over the course of rest. In persons with chronic physical overexertion, changes in the binding capacity of transcortin in the process of physical exertion are not observed.

3. In the period of physical exertion, in healthy untrained people and athletes with chronic physical overexertion, the blood content of protein-bound hormones remains unchanged, which leads to an increase in the plasma of free, biologically active forms of corticosteroids.

CHANGE IN THE BINDING CAPACITY OF TRANSCORTIN, CONTENT OF TOTAL 11-OCS,  
THEIR BINDING WITH PROTEIN AND FREE FORMS IN PLASMA OF THE PERIPHERAL BLOOD  
UNDER THE INFLUENCE OF PHYSICAL EXERCISE (In mkg%).

Group of Subjects	Binding Capacity of Transcortin				11-OCS			
					Total Concentration			
	Control Data	First Day	Third Day	Fourth Day	Control Data	First Day	Third Day	Fourth Day
	I	II	III	IV	I	II	III	IV
Healthy athletes	28,3±0,6	—	25,1±1,5	21,5±2,5	26,9±1,7	—	21,3±2,0	24,3±3,3
Athletes with chronic physical overexertion	24,05±0,8 $P<0,001$	$P_{I-II} \left\{ \begin{array}{l} >0,5 \\ <0,01 \end{array} \right.$ 25,2±2,5	$P_{I-II} \left\{ \begin{array}{l} >0,5 \\ <0,01 \end{array} \right.$ 26,3±2,6	23,2±1,8	25,8±1,3	26,0±2,5	28,7±1,3	25,4±2,0
Healthy untrained people (control group)	28,3±2,2	25,6±2,6 $P_{I-II} \left\{ \begin{array}{l} >0,5 \\ <0,01 \end{array} \right.$ $P_{I-III}$ $P_{I-IV}$	28,6±3,4	28,8±8,9	23,8±0,9	24,6±1,9	26,4±2,6	25,1±3,2

  

Group of Subjects	11-OCS							
	Forms Bound with Protein				Free Forms			
	Control Data	First Day	Third Day	Fourth Day	Control Data	First Day	Third Day	Fourth Day
	I	II	III	IV	I	II	III	IV
Healthy athletes	23,6±1,2 $P<0,001$	—	18,7±1,7	21,5±3,1	3,2±0,6	—	2,6±0,5	3,7±0,9
Athletes with chronic physical overexertion	21,7±0,7	19,6±2,7	21,4±2,8 $P_{I-II} \left\{ \begin{array}{l} >0,5 \\ <0,05 \end{array} \right.$ $P_{I-III}$ $P_{I-IV}$	19,9±1,2 $P_{I-III} <0,05$	5,5±0,6 $P<0,001$	6,4±1,2 $P<0,01$	10,3±1,7	5,5±1,0
Healthy untrained people (control group)	20,5±0,7	19,3±3,2	19,7±4,3	19,0±7,5 $P_{I-II} \left\{ \begin{array}{l} >0,5 \\ <0,05 \end{array} \right.$ $P_{I-III}$ $P_{I-IV}$	2,4±0,6 $P<0,001$	6,4±1,7	6,7±2,5	4,0±2,6

Commas indicate decimal points.

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